PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	The article features a meta-analysis of Sleep Onset Latency and Sleep Duration in Prader-Willi Syndrome, accompanied by an extensive literature review of the research concerning the sleep and eating phenotypes of the Prader-Willi and Angelman syndromes and the evolutionary, physiological and genetic background knowledge and models which we argue to be necessary to understand the full implications of these results.	1
ABSTRACT			
Structured summary	2	Sleep Onset Latency is measure of the time spent settling into nocturnal sleep, which can be assessed either with polysomnography, actigraphy or visual assessments. Similarly, Sleep duration is a measure of the total time spent asleep during the night and is most accurately assessed through polysomnography or actigraphy. Both Sleep Onset latency and Sleep duration are altered in numerous neurodevelopmental disorders. However, previous studies provide conflicting results of how Sleep Onset Latency and Sleep Duration are altered in Prader-Willi Syndrome as compared to typical development. We set out to conduct a brief meta-analysis of Sleep Onset Latency and Sleep Duration in Prader-Willi Syndrome as compared to typically developing individuals. We chose two public scientific databases, Pubmed and Web of Science for our approach. Original research articles featuring quantitative measures of the sleep phenotypes in Prader-Willi Syndrome. Eligible studies were assessed for accurate measures of Sleep Onset Latency and Sleep duration in comparison to typically developing individuals (controls) and these results were incorporated into a meta-analysis of the respective traits in Prader-Willi Syndrome. We found Sleep Onset Latency shows a small but significant negative effect in Prader-Willi Syndrome, while Sleep Duration was not shown to be significantly different from typically developing individuals. Our results are limited by a small number of studies with low sample sizes and varying methods and age groups. However, each study featured its own control group of typically developing individuals and only the effect size between Prader-Willi syndrome and typical development was assessed in the meta-analysis. We conclude that Prader-Willi Syndrome may alter the phenotype of Sleep Onset Latency which along with our review of the sleep and eating phenotypes in Prader-Willi and Angelman syndromes, implicates the effect genomic imprinting and intragenomic conflict in regulation of sleep rhythms and eating.	-
INTRODUCTION			
Rationale	3	Sleep onset Latency is recognized as an indicator of a healthy sleep rhythm and both positive and negative deviations of sleep onset latency may indicate sleep disorders, respectively insomnia or excessive daytime sleepiness. Sleep duration is directly affected by Sleep onset latency and may indicate problems with falling asleep, night waking, or early waking and as such has clear implications for the individual's mood and ability to function.	-
Objectives	4	The group eligible for the study features individuals who have been diagnosed with Prader-Willi syndrome, and have participated in a published scientific study with quantitative measurements of sleep onset latency or sleep duration. The comparison groups consist of age-matched, typically developing individuals chosen for the purposes of each of the original studies. We intend to assess whether previously published studies indicate that sleep onset latency and	4

PRISMA 2009 Checklist

		sleep duration are significantly altered in Prader-Willi Syndrome in comparison to typical development. Our results will have implications for future studies concerning sleep phenotypes in Prader-Willi syndrome and other neurodevelopmental syndromes.	
METHODS			
Protocol and registration	5	*Not applicable*	-
Eligibility criteria	6	Original research articles featuring objective measurements of sleep phenotypes in individuals diagnosed with Prader-Willi syndrome were considered eligible for the study. We limited our search to scientific studies written in English, published before May 2018. Furthermore, we limited the scope of our analysis to studies which featured a direct comparison to a control group of typically developing individuals to characterize the phenotypes of the traits and how these traits are altered in Prader-Willi Syndrome.	4
Information sources	7	We searched the full records both Pubmed and Web of Science databases as 3rd of May 2018. Additionally, previous meta-analyses and reviews concerning sleep phenotypes in Prader-Willi syndromes were assessed to cover the full scope of previous studies.	4
Search	8	The search terms applied were “Sleep AND Prader-Willi”.	4
Study selection	9	All search results from both databases were screened for original research articles which fulfilled our full eligibility criteria and all eligible studies were incorporated into the meta-analysis.	4
Data collection process	10	Results were extracted directly from published articles. In cases where data was reported only with the ranges and medians of the relevant sleep traits, the mean and the standard deviation of these parameters were estimated based on the procedures described in the article.	4
Data items	11	The data items collected included a measure of *Sleep Onset Latency, Sleep Latency* or *Time spent falling asleep* or alternatively, *Sleep Duration,* measured in minutes or hours and minutes.	4
Risk of bias in individual studies	12	Each of the originally published articles concern studies with a broad focus on characterizing the sleep disorders typical to Prader-Willi Syndrome based on objective measurements of the entire sleep phenotype and as such, we do not expect the results to contain significant bias in regards to any singular sleep trait.	4, 9, 10
Summary measures	13	We chose Hedge’s G as our principal summary measure, estimated with a fixed-effect model. This measure describes the deviation of the relevant sleep traits between individuals with Prader-Willi Syndrome as compared to typically developing individuals.	4
Synthesis of results	14	Consistency of the results across studies was assessed with a test of heterogeneity, measured with the Q test and we have indicated the heterogeneity seen in the results in our synthesis.	9, 10

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Risk of bias across studies	15	Publication bias in among any individual studies was evaluated using a weighted regression test, as is also indicated in the article. We take any publication bias into consideration regarding the validity of our results and their implications, while the full data is presented here as it was published in the original studies.	

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Additional analyses	16	No additional analyses are presented here, as we've reasoned that due to small number of studies and low sample sizes, a focused analysis with a fixed-effect model would be the most appropriate approach.	
RESULTS			
Study selection	17	A total of 371 search results on Web of Science and 208 search results Pubmed were screened and assessed individually for eligibility. Furthermore, 25 studies which had been previously featured in meta-analyses concerning sleep phenotypes in Prader-Willi syndrome were considered for the purposes of our analysis. After initial screening, a total of 32 studies featuring original research on the nocturnal sleep phenotype in Prader-Willi Syndrome were considered for our analysis. Finally, we limited our analysis to studies that featured a comparison to an age-matched control group. A total of 7 studies for Sleep onset latency and 6 studies for Sleep duration were incorporated	
Study characteristics	18	The study characteristics of each study are presented in table 2. provided as supplemental data.	
Risk of bias within studies	19	Assessments for risk of bias in any of the individual studies have not been made available in any of the original studies.	
Results of individual studies	20	Results of the individual studies are indicated as effect sizes in figure 3, and shown here with appropriate citations and references	
Synthesis of results	21	The results of the analyses are reported in the article and presented in further detail in the supplementary data. We found that sleep onset latency shows a small but significant negative effect in Prader-Willi Syndrome, while Sleep duration was not found significantly different from that of typically developing individuals. Secondly, both Sleep duration and sleep onset latency showed significant heterogeneity across the studies, which we attribute to the limited sizes of the study populations.	
Risk of bias across studies	22	We found no indication of any significant publication bias in our analysis.	
Additional analysis	23	No additional analyses are presented here, as we've reasoned that due to small number of studies and low sample sizes, a focused analysis with a fixed-effect model would be the most appropriate approach.	
DISCUSSION			
Summary of evidence	24	While the heterogeneity of the relevant traits across the studies must be taken into consideration regarding the results of our analysis, our analysis indicates that according to currently available and relevant studies, sleep onset latency in Prader-Willi Syndrome shows small but significant negative effect. We found no evidence for significant deviations in either direction with sleep duration.	
Limitations	25	We consider our analysis is limited by the small number eligible studies and low sample sizes. Furthermore, incomplete retrieval of eligible research may be plausible due to lack of an independent replication in our search and screening procedures.	
Conclusions	26	Our results indicate Sleep Onset Latency may be shortened in Prader-Willi syndrome as compared to typically developing individuals and as such, may be opposite to how the phenotype of this trait is altered in Angelman Syndrome. The evolutionary and physiological implications of these results are discussed in detail in the article.	
FUNDING			
Funding	27	This work was funded on the NSERC research grant (No. 06505) and the design of this meta-analysis has not been influenced by the funding source in any way.	

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